

A Model of Aging and a Shape of the Observed Hazard Rate

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Abstract

A probabilistic model of biological aging is considered. It is based on the assumption that a random resource, a stochastic process of aging (wear) and the corresponding anti-aging process are embedded at birth. A death occurs when the accumulated wear exceeds the initial random resource. It is assumed that the anti-aging process decreases wear in each increment. The impact of environment (lifestyle) is also taken into account. The corresponding relations for the observed and the conditional hazard rate are obtained. Similar to some demographic models, the deceleration of mortality phenomenon is explained via the concept of frailty.

1. Introduction

There is an enormous literature on biological theories of aging. Various stochastic mortality models are reviewed, for instance, in Yashin *et al.* (2000). The nature of human aging is in some “biological wearing”. There are different probabilistic ways to model wear. The simplest way of modeling is just to describe the corresponding lifetime random variable T by its distribution function $F(t)$. One of the standard demographic models is the Gompertz model for human mortality with exponentially increasing hazard rate $\lambda(t)$:

$$F(t) = 1 - \exp\left\{-\frac{\alpha}{\beta} \exp\{\beta t\}\right\}, \quad \lambda(t) = \alpha \exp\{\beta t\}, \quad \alpha > 0, \beta > 0 \quad (1)$$

It is already a well-known fact that along with mortality increase with age (according to (1), for instance) the subsequent mortality leveling-off takes place. In a recent paper by Gavrilov and Gavrilova (2001) the following reliability model of human aging was suggested. It was assumed that organisms consist of a series structure of redundant blocks. Each block consists of a random number (in parallel) of initially “operable” components with a constant hazard rate λ . The authors considered Poisson and binomial distributions for describing this random redundancy. It turned out that for both cases the resulting hazard rate exponentially increases (as in (1)) for sufficiently small t and as $t \rightarrow \infty$ it asymptotically converges to λ from below. The latter fact is obvious, because as $t \rightarrow \infty$ (on condition that the block is operable) probability that only one component is operable tends to 1. It can be shown that the first one is the consequence of the Poisson assumption (or the Poisson approximation for the binomial distribution). The shape of $\lambda(t)$ can differ from exponential for other types of governing distributions. One can consider this problem also like a problem of characterizing the hazard rate of objects with unknown (random) initial age. It can be shown that under certain assumptions the resulting hazard rate can initially decrease even if the hazard rate of the governing distribution is increasing. The idea of some initial resource given to the object by birth will be generalized further.

2. Modeling wear

Consider the following setting. An object starts functioning at $t = 0$ in some deterministic environment. $z(t)$, where $z(t)$ is a vector of environmental (stress) parameters. Assume that in the process of

production (engineering applications) or birth (biological applications) it had acquired an initial unobserved random resource R with a DF $F_0(r) : F_0(r) = P(R \leq r)$.

Suppose that for each realization of R the run out resource $W(t)$ to be called wear monotonically increases. Assume that the wear increment in $[t, t + dt)$ is defined as $\tilde{w}(z(t), W(t))dt + o(dt)$, where $\tilde{w}(z(t), W(t)) \equiv w(t) > 0$ is a deterministic functional. Let additionally $W(0) = 0$ and $W(t) \rightarrow \infty$ as $t \rightarrow \infty$. It is clearly seen that under these assumptions we arrive at the accelerated life model (ALM):

$$P(T \leq t) \equiv F(t) = F_0(W(t)) \equiv P(R \leq W(t)); \quad W(t) = \int_0^t w(u)du; \quad w(t) > 0; \quad t \in [0, \infty). \quad (2)$$

where $F_0(t)$ is an absolutely continuous DF (the case of the discrete R can be also considered).

As follows from (2), the failure (death) occurs when the wear $W(t)$ reaches a random R . This equation describes a *deterministic* diffusion with a random threshold. It is natural to model a *random* wear by a monotonically increasing stochastic process $W_t, t \geq 0$ as, for instance, in Lemoine and Wenocur, (1985):

$$W_{t+\Delta t} - W_t = a(W_t)\varepsilon(\Delta t) + b(W_t)\Delta t, \quad \forall t \in [0, \infty), \quad (3)$$

where $\varepsilon(\Delta t)$ is a random variable with a positive support and finite first two moments, and $a(\cdot)$, $b(\cdot)$ are continuous positive functions of their arguments. Letting $\Delta t \rightarrow 0$, the continuous version of this equation can be obtained in the form of the Ito stochastic differential equation.

Substituting the deterministic wear $W(t)$ in (2) by the increasing stochastic process $W_t, t \geq 0$ leads to the following relation:

$$F(t) = P(T \leq t) = P(R \leq W_t) = E[F_0(W_t)] = F_0(\bar{W}(t)), \quad (4)$$

where the expectation is taken with respect to $W_t, t \geq 0$ and $\bar{W}(t)$ denotes some averaged (equivalent) deterministic wear. The distribution function $F_0(W_t)$ should be understood conditionally: $F(t | W_t) = P(T \leq t | W_t, 0 \leq u \leq t)$, where $W_t, 0 \leq u \leq t$ is the history of this stochastic process.

Let, as previously, $\lambda(t)$ denotes the hazard rate (the *observed* hazard rate), which corresponds to the DF $F(t)$. From (4), using the results of Yashin and Manton (1997) the following important relationship between the observed and the conditional hazard rates exists:

$$\lambda(t) = E[w_t \lambda_0(W_t) | T > t], \quad (5)$$

where w_t denotes the stochastic rate of diffusion: $dW_t \equiv w_t dt$ and the hazard rate $\lambda_0(t)$ characterizes DF $F_0(t)$. Equation (5) can be used for analyzing the shape of $\lambda(t)$, and this is very important in demographic studies, for instance.

Example. Let $\lambda_0 = 1$ and consider a specific case of the process of wear: $W_t = w_t = \varphi k \exp\{t\}$, where $k > 0$ is a constant and φ is an exponential random variable with parameter ϑ (Finkelstein and Esaulova 2001). Thus, the mixture (observed) hazard rate is obtained by mixing the truncated extreme value distribution (Gompertz law (1) in demography):

$$E[w_t | T > t] = \lambda(t) = \frac{k \exp\{t\}}{k \exp\{t\} - k + \vartheta} = 1 + \frac{k - \vartheta}{k \exp\{t\} - k + \vartheta}.$$

When $k > \vartheta$, the mixture hazard rate $\lambda(t)$ is monotonically decreasing, asymptotically converging to 1. For $k < \vartheta$ it is monotonically increasing, asymptotically converging to 1. Hence, mixing of the DF, with a sharply increasing hazard rate can even result in the distribution with a decreasing failure rate!

This example shows that the operation of conditional expectation (mixing) can result in a significantly different pattern of degradation at the individual and population level, and this leads to the mentioned above deceleration in the mortality rate.

3. Aging and anti-aging

Assume now that there exist two processes: aging and anti-aging (regeneration) to be modeled by stochastic processes of wear and anti-wear, respectively. Denote the resulting stochastic process (unobserved) with independent increments by W_t^p . Let the process of anti-wear decreases each increment of wear according to the following rule, which generalizes model (3):

$$\begin{aligned} W_{t+\Delta t}^p - W_t^p &= a(W_t) \varepsilon(\Delta t) + b(W_t) \Delta t - \rho(t) [a(W_t) \varepsilon(\Delta t) + b(W_t) \Delta t] \\ &= (1 - \rho(t)) [a(W_t) \varepsilon(\Delta t) + b(W_t) \Delta t], \quad \forall t \in [0, \infty) \end{aligned}$$

where $\rho(t) : 0 \leq \rho(t) \leq 1$ is a decreasing (non-increasing) function (the case of a decreasing stochastic process $\rho_t, t \geq 0$ can be considered as well). Let $\rho(t) \rightarrow 0$ as $t \rightarrow \infty$. This function describes the ability of an object to decrease its wear in each increment. Similar to the previous section, biological aging can be modeled by the process W_t^p . Aging for humans actually starts at the age of maturity: 25-30 years. It means that $\rho(t)$ is very close or equal to 1 up to this age. Alternatively the combined process of wear and anti-wear can be also defined directly via the rate of diffusion w_t :

$$w_t^p = (1 - \rho(t)) w_t, \quad (6)$$

which means that the rate of diffusion is smaller due to anti-aging by the time-dependent factor $(1 - \rho(t))$. Thus, the formulas of the previous section can be written substituting w_t by w_t^p and W_t

by $W_t^p = \int_0^t (1 - \rho(u)) w_u du$. Relation (5), for the case of stochastic $\rho_t, t \geq 0$, for instance, turns to

$$\lambda(t) = E[(1 - \rho_t) w_t \lambda_0(W_t^p) | T > t]. \quad (7)$$

Assume that the human lifetime is programmed genetically at birth by the triple $\{R, \hat{w}_t, \hat{\rho}_t\}$, where \hat{w}_t and $\hat{\rho}_t$ are the “stochastic programs”, which exhibit themselves in the future real time as the *baseline stochastic processes* w_t and ρ_t . The realizations of these stochastic programs $\hat{w}(t)$ and $\hat{\rho}(t)$ (as well as the realization of R) are embedded individually at birth. Let $R, \hat{w}_t, \hat{\rho}_t$ be stochastically independent. Given the corresponding realization (in real time) $r_0, w(t), \rho(t)$, the time of death t_d is defined uniquely from the equation:

$$r_0 = \int_0^{t_d} (1 - \rho(u)) w(u) du. \quad (8)$$

and can be solved explicitly for some simple specific cases. The genetic interpretation of dependency between different triples (e.g. non related individuals, monogzygotic and dizygotic twins) is discussed in Finkelstein (2002).

In the frame of our “triple mode” the following interesting question arises: what is more important in defining the time of death: the initial resource R or the process of anti-wear defined by $\rho(t)$ ($\rho_t, t \geq 0$)? It can be shown (Finkelstein, 2002) that if $\rho(t)$ sharply decreases to 0 (bad anti-aging mechanism) then the impact of the initial resource is dominating, whereas the answer is opposite when $\rho(t)$ is close to 1 up to sufficiently large t (good anti-aging mechanism).

Let the aging and anti-aging processes depend for simplicity on one overall environmental (*lifestyle*) scalar parameter $\theta(t) : w_t(\theta(t)), \rho_t(\theta(t))$. Assume, simplifying further, that $\theta(t) \equiv \theta > 0$ is constant in time and θ_g stands for a “good” lifestyle and θ_b , for a “bad” lifestyle; $\theta_g < \theta_b$. It is natural to assume that in realizations:

$$\rho(t, \theta_g) > \rho(t, \theta_b), w(t, \theta_g) < w(t, \theta_b), \forall t \in (0, \infty),$$

The accelerated life model is a natural choice for $\rho(t, \theta)$ and $w(t, \theta) : w(t, \rho, \theta) \equiv (1 - \rho(\theta t)) w(\theta t)$.

Let for convenience: $0 < \theta_g < 1 < \theta_b$ and $t_d(\theta)$ denote the time of death in a realization with a scale parameter θ . Then, using the equation similar to (8) for the time of death $t_d(\theta)$, and assuming the form of the step function (with a jump at $t = \tilde{t}$) for $\rho(t, \theta)$ one can easily derive (Finkelstein 2002):

$$t_d(\theta_g) - t_d(\theta_b) \approx \tilde{t} \left(\frac{\theta_b - \theta_g}{\theta_b \theta_g} \right).$$

Therefore, if \tilde{t} is sufficiently large and $\theta_b - \theta_g$ is not too small, and this is quite realistic in practice, then we can say that (given all assumptions) the impact of a lifestyle far exceeds the impact of r_0 .

4. The shape of the observed hazard rate

Similar to (7) we can define the lifestyle-dependent observed hazard rate:

$$\lambda(t) = E[w_t^p(\theta(t)) \lambda_0(W_t^p(\theta(t)) | T > t)]. \quad (9)$$

Humans experience degradation with age. Therefore it is reasonable to assume that this individual degradation leads to an increasing individual hazard rate, which corresponds to increasing realizations of the hazard rate process $w_t^p(\theta(t)) \lambda_0(W_t^p(\theta(t)))$ (In the absence of information on $F_0(t)$ the reasonable choice is exponential or truncated normal distribution). What can be said then about the monotonicity properties of the conditional expectation (9)? Without conditioning, the operation of expectation would result in some increasing mean hazard rate. As t increases, conditioning on $T > t$ implies that the weight of realizations with higher value of the hazard rate is gradually decreasing: weaker populations are dying out first! The output of this process can result in slowing down the rate with which the observed hazard rate $\lambda(t)$ increases or even in it's decreasing, as was shown in Example.

Due to our assumptions, $1 - \rho(t, \theta(t))$ tends to 1 as t increase. This is another source for slowing down the increase in $\lambda(t)$ for sufficiently large t . The third source is in the environment that was assumed to be deterministic. This means that another random factor intervenes, and this fact "increases the frailty in the model". Thus there are three sources for the deceleration of mortality in the model:

- a. Stochastic nature of the aging process.
- b. Anti-aging process (it inputs in deceleration even if it is deterministic)
- c. Stochastic environment.

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